

CLAIMS

1. A method of measuring a solubility of a protein with respect to a concentration of the precipitating agent, comprising observing interference fringes formed around a protein crystal using a two-beam interferometer while increasing or decreasing the concentration of the precipitating agent in the protein solution filled around the protein crystal, wherein the concentration of the protein solution filled around the protein crystal is measured and the interference fringes are observed.

2. The method of measuring a solubility of a protein with respect to a concentration of the precipitating agent according to claim 1, wherein the method comprises: providing a quartz thin plate having a light reflecting thin film on a portion of the front side surface or back side surface thereof; mounting the protein crystal on a portion of the quartz thin plate where the light reflecting thin film is provided; observing the interference fringes formed around the protein crystal; and measuring the concentration of the protein in the protein solution through a portion of the quartz thin plate where light reflecting thin film is not provided, whereby performing measurement of the concentration of the protein solution filled around the protein crystal and observation of the interference fringes.

3. The method according to claim 1 or 2, wherein the concentration of the precipitating agent in the protein solution filled around the protein crystal is increased or decreased by adjusting the concentration of a contained precipitating agent

solution separated from the protein solution via a dialysis membrane.

4. The method according to any one of claims 1 to 3, wherein the solubility of the protein is determined from the concentration of the protein solution and the concentration of the precipitating agent when the interference fringes formed around the protein crystal observed using the two-beam interferometer are constituted by straight lines that do not curve in the vicinity of the protein crystal.

5. The method according to any one of claims 1 to 4, wherein the concentration of the protein in the protein solution is measured by a spectrophotometer.

6. A method of preparing a solubility curve of a protein with respect to a concentration of a precipitating agent, comprising: changing stepwise a concentration of a protein in a protein solution filled around a protein crystal; and obtaining a plurality of solubilities by repeating the measurement of the solubility described in any one of claims 1 to 5.

7. The method according to claim 6, wherein the solubility curve is prepared by continuously performing the stepwise change of the concentration of the protein solution filled around the protein crystal.

8. The method according to any one of claims 1 to 7, wherein the two-beam interferometer is a Michelson type two-beam

interferometer.

9. An apparatus of measuring a solubility of a protein with respect to a concentration of the precipitating agent, comprising: a dialysis cell having a container for containing a protein crystal and a protein solution filled around the protein crystal, and providing with a dialysis membrane; means for measuring a concentration of the protein solution; a two-beam interferometer for observing interference fringes around the protein crystal; means for increasing or decreasing a concentration of the precipitating agent in the protein solution filled around the protein crystal in the dialysis cell; and means for measuring the concentration of the precipitating agent in the protein solution filled around the protein crystal in the dialysis cell.

10. The apparatus according to claim 9, wherein the dialysis cell comprises: a quartz thin plate for mounting the protein crystal, having a light reflecting thin film on a portion of the front side surface or back side surface thereof; an inner vessel containing the quartz thin plate therein, provided with a surface portion covered with a dialysis membrane and filled with the protein solution therein; and an outer vessel filled with the precipitating agent solution outside the dialysis membrane.

11. The apparatus according to claim 9 or 10, wherein the means for measuring the concentration of the protein solution is a spectrophotometer.

12. The apparatus according to claim 11, wherein the spectrophotometer measures an intensity of transmitted light that transmits a portion of the quartz thin plate in the dialysis cell where light reflecting thin film is not provided.

13. The apparatus according to any one of claims 9 to 12, further comprising means for sending the precipitating agent solution to the outer vessel of the dialysis cell while continuously increasing or decreasing the concentration of the precipitating agent.

14. The apparatus according to any one of claims 9 to 13, further comprising means for introducing the protein solution having a desired concentration or a diluent solution into the inner vessel of the dialysis cell without disassembling the dialysis cell.

15. The apparatus according to any one of claims 9 to 14, further comprising means for photographing the interference fringes by the two-beam interferometer, such as a CCD camera.

16. The apparatus according to any one of claims 9 to 15, wherein the two-beam interferometer is a Michelson type two-beam interferometer.

17. A dialysis cell for an apparatus for measuring a solubility of a protein, comprising: a quartz thin plate for mounting the protein crystal, having a light reflecting thin film on a portion of the front side surface or back side surface thereof; an inner vessel for containing the quartz thin plate, provided with a

surface portion covered with a dialysis membrane and filled with the protein solution therein; and an outer vessel filled with the protein precipitating agent solution outside the dialysis membrane.

18. A method of producing a protein crystal by utilizing a solubility curve prepared by the method according to claim 6 or 7 while controlling a degree of supersaturation of a protein solution around a growing protein crystal.

19. An apparatus of producing a protein crystal, comprising: a dialysis cell having a container for containing a protein crystal and a protein solution filled around the protein crystal, and provided with a dialysis membrane; means for controlling a concentration of the protein in the protein solution around the protein crystal; means for measuring a concentration of the protein solution around the protein crystal; a two-beam interferometer for observing interference fringes around the protein crystal; means for controlling a concentration of the precipitating agent in the protein solution around the protein crystal; and means for measuring the concentration of the precipitating agent in the dialysis cell.

20. The apparatus according to claim 19, wherein the dialysis cell comprises: a quartz thin plate for mounting the protein crystal, and provided a light reflecting thin film on a portion of the front side surface or back side surface thereof; an inner vessel for containing the quartz thin plate therein, provided with a surface portion covered with a dialysis membrane and filled

with the protein solution therein; and an outer vessel filled with the protein precipitating agent solution outside the dialysis membrane.

21. The apparatus according to claim 19 or 20, wherein the means for measuring the concentration of the protein solution is a spectrophotometer.

22. The apparatus according to claim 21, wherein the spectrophotometer measures an intensity of transmitted light that transmits a portion of the quartz thin plate in the dialysis cell where light reflecting thin film is not provided.

23. The apparatus according to any one of claims 19 to 22, further comprising means for sending the precipitating agent solution having a desired concentration to the outer vessel of the dialysis cell.

24. The apparatus according to any one of claims 19 to 23, further comprising means for introducing the protein solution having a desired concentration into the inner vessel of the dialysis cell without disassembling the dialysis cell.

25. The apparatus according to any one of claims 19 to 24, further comprising means for photographing the interference fringes by the two-beam interferometer, such as a CCD camera.

26. The apparatus according to any one of claims 19 to 25, wherein the two-beam interferometer is a Michelson type two-beam

interferometer.

27. A dialysis cell for an apparatus for producing a protein crystal, comprising: a quartz thin plate for mounting the protein crystal; and provided a light reflecting thin film on a portion of the front side surface or back side surface thereof; an inner vessel for containing the quartz thin plate therein, provided with a surface portion covered with a dialysis membrane and filled with the protein solution therein; and an outer vessel filled with the protein precipitating agent solution outside the dialysis membrane.